=> b reg
FILE 'REGISTRY' ENTERED AT 18:01:49 ON 08 AUG 2007
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STRUCTURE FILE UPDATES: 7 AUG 2007 HIGHEST RN 944239-85-4 DICTIONARY FILE UPDATES: 7 AUG 2007 HIGHEST RN 944239-85-4

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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http://www.cas.org/support/stngen/stndoc/properties.html

=> d que sta 110
L8

STR

2 7 10
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1 C C 11 12 13 @14 15

VAR G1=AK/O/S/N/14 NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED ECOUNT IS E6 C AT 11 ECOUNT IS E5 C E1 N AT 13

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE L10 40 SEA FILE=REGISTRY SSS FUL L8

100.0% PROCESSED 108196 ITERATIONS SEARCH TIME: 00.00.04

40 ANSWERS

=> b hcap
FILE 'HCAPLUS' ENTERED AT 18:02:31 ON 08 AUG 2007
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FILE COVERS 1907 - 8 Aug 2007 VOL 147 ISS 7

FILE LAST UPDATED: 7 Aug 2007 (20070807/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitrn fhitstr 113

- L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
- AN 2005:409508 HCAPLUS
- DN 142:463726
- TI Preparation of benzimidazolyls as TIE-2 tyrosine kinase inhibitors for the treatment of tumors
- IN Staehle, Wolfgang; Buchstaller, Hans-Peter; Jonczyk, Alfred; Rautenberg, Wilfried
- PA Merck Patent G.m.b.H., Germany
- SO PCT Int. Appl., 105 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN	. CNT	1

GΙ

FAN.	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	WO2005042520	A1	20050512	2004WO-EP11550	20041014 <
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				DM, DZ, EC, EE, EG,	
	· · · · · · · · · · · · · · · · · · ·			IN, IS, JP, KE, KG,	
				MD, MG, MK, MN, MW,	
				RO, RU, SC, SD, SE,	
	TJ, TM,	TN, TR, TT	, TZ, UA,	UG, US, UZ, VC, VN,	YU, ZA, ZM, ZW
	RW: BW, GH,	GM, KE, LS	, MW, MZ,	NA, SD, SL, SZ, TZ,	UG, ZM, ZW, AM,
	AZ, BY,	KG, KZ, MD	, RU, TJ,	TM, AT, BE, BG, CH,	CY, CZ, DE, DK,
	EE, ES,	FI, FR, GB	, GR, HU,	IE, IT, LU, MC, NL,	PL, PT, RO, SE,
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		Al	20050512		20041014 <
	EP1675849		20060705		20041014 <
				GB, GR, IT, LI, LU,	
				TR, BG, CZ, EE, HU,	
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	BR2004015760	A	20061219		20041014 <
		Τ.	20070412		
	MX2006PA04405	A	20060614		
		A1 A	20070322		20060424 <
DD 3 T	IN2006KN01239		20070427		20060311 <
PRAI	2003DE-1049587 2004WO-EP11550	A W	20031024		
os	MARPAT 142:46372	••	20041014	ζ	•
US	PMRFM1 142:403/2	· O			

AB Title compds. I [R = (R1)m; R1 = (R1')p; R2 = (R2')q; m, p, q = 0-4; R1, R1' = Halo, OH, CN, etc.; L = CH2, CH2CH2, O, etc.; R2' = halo, OH, CO2H, etc.; E, G, M, Q, U = C or N atom with provisos] and their

Ι

ΙI

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pharmaceutically acceptable salts and formulations were prepared For
     example, condensation of 4-(4-isothiocyanatophenoxy)puridine and
     4-nitro-1,2-phenylenediamine afforded claimed benzimidazol II. In TIE-2
     tyrosine kinase inhibition assays, 3-examples of compds. I exhibited IC50
     values ranging from 5-40 x 10-7 mol/L. Compds. I are claimed to be useful
     as tyrosine kinase inhibitors in the treatment of tumors.
     851677-12-8P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-
     (pyridin-4-yloxy)phenyl]amine 851677-13-9P, [4-(Pyridin-4-
     yloxy)phenyl](6-trifluoromethyl-1H-benzimidazol-2-yl)amine
     851677-14-0P, (6-Methyl-1H-benzimidazol-2-yl)[4-(pyridin-4-
     yloxy)phenyl)amine 851677-15-1P, (5-Chloro-4-methyl-1H-
     benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine 851677-16-2P,
     (4-Bromo-6-trifluoromethyl-1H-benzimidazol-2-yl) [4-(pyridin-4-
     yloxy)phenyl]amine 851677-17-3P, (4-Bromo-6-trifluoromethyl-1H-
     benzimidazol-2-yl) [4-(pyridin-3-yloxy)phenyl]amine 851677-18-4P, (5,6-Dimethyl-1H-benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine
     851677-19-5P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-
     (pyridin-3-yloxy)phenyl]amine 851677-20-8P, (5,6-Dichloro-1H-
     benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine 851677-21-9P,
     (5,6-Dichloro-1H-benzimidazol-2-yl)[4-(pyridin-3-yloxy)phenyl]amine
     851677-22-0P, (5-Chloro-1H-benzimidazol-2-yl) [4-(pyridin-4-
     yloxy)phenyl]amine 851677-23-1P, (5-Chloro-1H-benzimidazol-2-
     yl)[4-(pyridin-3-yloxy)phenyl]amine 851677-24-2P,
     (4-Methyl-1H-benzimidazol-2-yl)[4-(pyridin-3-yloxy)phenyl]amine
     851677-25-3P, (4-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-
     (pyridin-4-yloxy)phenyl]amine 851677-26-4P, (4-Chloro-6-
     trifluoromethyl-1H-benzimidazol-2-yl) [4-(pyridin-3-yloxy)phenyl]amine
     851677-27-5P, (4,5-Dimethyl-1H-benzimidazol-2-yl)[4-(pyridin-4-
     yloxy)phenyl]amine 851677-28-6P, (5-Chloro-6-methyl-1H-
     benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine 851677-29-7P,
     (5-Chloro-6-methyl-1H-benzimidazol-2-yl)[4-(pyridin-3-yloxy)phenyl]amine
     851677-30-0P, [4,6-Bis(trifluoromethyl)-1H-benzimidazol-2-yl][4-
     (pyridin-4-yloxy)phenyl]amine 851677-31-1P, [4,6-
     Bis(trifluoromethyl)-1H-benzimidazol-2-yl][4-(pyridin-3-yloxy)phenyl]amine
     851677-32-2P, [4-(Pyridin-3-yloxy)phenyl](6-trifluoromethyl-1H-
     benzimidazol-2-yl)amine 851677-33-3P, (6-Methyl-1H-benzimidazol-
     2-yl) [4-(pyridin-3-yloxy)phenyl]amine 851677-34-4P,
     (4,5-Dimethyl-1H-benzimidazol-2-yl) [4-(pyridin-3-yloxy)phenyl]amine
     851677-35-5P, (5-Chloro-4-methyl-1H-benzimidazol-2-yl)[4-(pyridin-
     3-yloxy)phenyl]amine 851677-36-6P, (4-Methyl-1H-benzimidazol-2-
     yl) [4-(pyridin-4-yloxy)phenyl]amine 851677-37-7P,
     (5,6-Dimethyl-1H-benzimidazol-2-yl)[4-(pyridin-3-yloxy)phenyl]amine
     851677-39-9P 851677-40-2P 851677-44-6P,
     (6-Nitro-1H-benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine
     851677-45-7P, 2-[4-(Pyridin-4-yloxy)phenylamino]-3H-benzimidazole-
     5-carboxlic acid methyl ester 851677-48-0P, (4-Fluoro-6-
     trifluoromethyl-1H-benzimidazol-2-yl)[4-(pyridin-4-yloxy)phenyl]amine
     851677-51-5P 851677-52-6P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of benzimidazolyls as TIE-2 tyrosine kinase inhibitors for the
        treatment of tumors)
     851677-12-8P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-
TT
     (pyridin-4-yloxy)phenyl]amine
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of benzimidazolyls as TIE-2 tyrosine kinase inhibitors for the
        treatment of tumors)
     851677-12-8 HCAPLUS
RN
     1H-Benzimidazol-2-amine, 5-chloro-N-[4-(4-pyridinyloxy)phenyl]-6-
CN
     (trifluoromethyl) - (9CI) (CA INDEX NAME)
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RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d bib abs hitstr 114 tot
     ANSWER 1 OF 4 HCAPLUS - COPYRIGHT 2007 ACS on STN
     2005:259680 HCAPLUS
ΑN
DN
     142:336356
     Preparation of benzimidazoles and imidazopyridines having affinity for
TΤ
     melanocortin (MC), in particular MC4, receptors
IN
     Poitout, Lydie; Brault, Valerie; Sackur, Carole; Roubert, Pierre; Plas,
     Pascale
PA
     U.S. Pat. Appl. Publ., 213 pp., Cont.-in-part of U.S. Ser. No. 504,033.
so
     CODEN: USXXCO
ידעו
     Patent
LA
     English
FAN.CNT 2
                                               APPLICATION NO.
                                                                        DATE
     PATENT NO.
                           KIND
                                  DATE
                           ----
PT.
     US2005065179
                           A1
                                  20050324
                                               2004US-0915920
                                               2003FR-0002320
     FR---2851563
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                                  20040827
                                                                        20030226
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                                  20050422
     WO2004075823
                            A2
                                  20040910
                                               2004WO-FR00418
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                                  20041007
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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              LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
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              MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
              GQ, GW, ML, MR, NE, SN, TD, TG
PRAI 2003FR-0002320
                           Α
                                  20030226
     2003US-0504033
                            A2
                                  20030920
     2004WO-FR00418
                                  20040225
                            W
     MARPAT 142:336356
```

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Title compds. I [wherein A = CH2, CO, (un) substituted COCH2; X = CH, N; R1, R2 = independently H, alkyl optionally substituted by OH, alkenyl, etc.; or R1NR2 = (un) substituted hetero(bi) cycloalkyl; R3 = alkyl, alkoxy, alkylthio, heteroaryl, (un) substituted hetero/cycloalkyl, aryl, etc.; R4 = (CH2)sR5; R5 = heterocycloalkyl, heteroaryl, etc.; s = 0-6) were prepared as melanocortin (MC), in particular MC4, receptor modulators (no data given). For example, II was prepared, in 2 steps, by amination of 3-Fluoro-N,N-bis(3-methylbutyl)-4-nitrobenzamide (preparation given) with 3-(piperidino)propylamine in CH3CN at reflux, followed by one-step hydrogenation/coupling with 4-acetylphenyl isothiocyanate. I are useful in the treatment of pathol. states and the diseases in which one or more melanocortin receptors are included such as pain, inflammatory conditions, etc.

848577-67-3P TT

OS

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of benzimidazoles and imidazopyridines having affinity for melanocortin (MC), in particular MC4, receptors)

RN 848577-67-3 HCAPLUS

1H-Benzimidazole-6-carboxamide, N, N-bis(3-methylbutyl)-1-[3-(1-CN piperidinyl)propyl]-2-[[4-(1-piperidinylsulfonyl)phenyl]amino]- (9CI) INDEX NAME)

GΙ

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ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
L14
     2004:817883 HCAPLUS
AN
DN
     141:332190
     Preparation of fused azoles such as 2,5-disubstituted benzimidazoles,
ΤI
     benzoxazoles and benzothiazoles as kinase inhibitors
     Dipietro, Lucian V.; Harmange, Jean-Christophe; Askew, Benny C., Jr.;
IN
     Elbaum, Daniel; Germain, Julie; Habgood, Gregory J.; Kim, Joseph L.;
     Patel, Vinod F.; Potashman, Michele; Van der Plas, Simon
     Amgen Inc., USA
PA
ŞΟ
     PCT Int. Appl., 289 pp.
     CODEN: PIXXD2
DT
     Patent
LΆ
     English
FAN.CNT 1
                                                                       DATE
     PATENT NO.
                          KIND
                                  DATE
                                              APPLICATION NO.
                                  20041007
                                                                       20040322
ΡI
     WO2004085425
                           Αl
                                              2004WO-US08809
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             GE, GH, GM, HR, HU, ID,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
                          PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
                      OM.
             NO, NZ,
                              TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
             TJ, TM, TN,
                          TR.
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             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
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                                               2004US-0804915.
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     2004US-0804915
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     2004WO-US08809
                                  20040322
     MARPAT 141:332190
os
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$$\begin{array}{c|c}
R^2 & Y^2 \\
 & Y^1 & Y^1
\end{array}$$

Title compds. I [W, X, Y1 and Y2 independently = O, S(O)n and NR3; ring A AB optionally contains a N atom at a non-fused, non-substituted ring position; n = 0-2; R = (un) substituted-aryl, -heterocyclyl, -fused heterocyclyl, etc.; R1 = (un)substituted-aryl, -arylalkyl, -heterocyclyl, etc.; R2 = H, halo, alkoxy, etc.; R3 = H or alkyl] are prepared and disclosed as having kinase inhibitory activity, such as VEGFR/KDR inhibitory activity. Thus, e.g., II was prepared by cyclocondensation of 4-(pyridin-4-yloxy)benzene-1,2-diamine with 1-chloro-4-isothiocyanato-2trifluoromethylbenzene. In human umbilical vein endothelial cell proliferation assay, selected I inhibited VEGF-stimulated proliferation at a level below 100 nM. Accordingly, I would be useful in the prevention and treatment of angiogenesis related disorders, ophthalmol. conditions, proliferative diseases, inflammatory diseases, and other pathol. conditions as described in the specification.

769960-08-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of benzimidazole, benzoxazole and benzothiazole derivs. as kinase inhibitors)

RN 769960-08-9 HCAPLUS

2-Pyridinecarboxamide, N-methyl-4-[[2-[[4-[1-methyl-1-(1-methyl-4-piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]- (9CI) (CA CN INDEX NAME)

THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 11 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN 2004:513393 HCAPLUS L14

AN

DN 141:71544

Preparation of substituted benzazoles as Raf kinase inhibitors TI

Amiri, Payman; Fantl, Wendy; Levine, Barry Haskell; Poon, Daniel J.; Ramurthy, Savithri; Renhowe, Paul A.; Subramanian, Sharadha; Sung, Leonard

PA

U.S. Pat. Appl. Publ., 476 pp., Cont.-in-part of U.S. Pat. Appl. 2004 so 87,626.

	CODEN:	USAA																
DT	Patent																	
LA	English																	
FAN.	CNT 2																	
		TENT NO.					APPL:	ICAT	ION I	NO.		DATE						
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ΡI		32004122237								20030929 20030331								
		4087626							20031		20030331							
	US70					B2 20060704				2004	. r	0004	۰.					
	AU20042				A1 20050414									20040929				
	CA25													20040929				
	WO2005032548								2004									
	₩:									BB,								
										DZ,								
										IS,								
•										MG,								
										RU,								
										US,								
	RW:									SD,								
										ΑT,								
										IT,								
•		SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝĒ,	
		SN,	TD,	TG														
	EP16									2004EP-0789345 GB, GR, IT, LI, LU, NL,								
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		ΙE,	SI,	FI,	RO,	CY,				EE,								
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	CN19						2007	0214	CN 2004-80032677						20040929			
	JP20075	0742	8		T		20070329		2006JP-0528331						20040929			
	MX2006P	A034	35		Α		20060620		2006MX-PA03435						20060327			
					Α	A 20060727			2006JP-0096143						20060330			
	IN2006K	800 <i>r</i>	38		Α		2007	0413	2006IN-KN00838						2	0060	405	
PRAI	2002US-	3690	66P		P		2002	0329										
	2003US-	0405					2003	0331										
	2003JP-	0579					2003	0331										
	2003US-	0675	927		Α		2003	0929										
	2004WO-	US32	161		W		2004	0929									•	

$$A^{1}$$
 R^{7}
 X^{2}
 X^{1}
 R^{3}
 R^{2}
 R^{2}
 R^{2}
 R^{3}
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 R^{3}
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 R^{5}
 R^{5}

MARPAT 141:71544

os GI CODEN: USXXCO

The title compds. I [wherein X1, X2 = N, NR4, O, S (with provisos); Y = O, S; A1 = (un)substituted alkyl, (hetero)cycloalkyl(alkyl), (hetero)aryl(alkyl), etc.; A2 = (un)substituted heteroaryl; R1 = O, H; R2 = NR5R6, OH; or CR1R2 = (un)substituted heterocycloalkyl, heteroaryl; R3 = H, halo, alkyl, alkoxy; R4 = H, OH, (di)alkylamino, alkyl; R5, R6 = H, (un)substituted (cyclo)alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, heterocyclyl, (hetero)aryl, etc.; or R5 and R6 are taken together to form (un)substituted heterocyclyl or heteroaryl; R7 = alkyl; and pharmaceutically acceptable salts, esters, or prodrugs] were prepared as Raf kinase inhibitors. Examples include synthetic methods and phys. data for 1400 compds., as well as descriptions of two Raf kinase bioassays. For instance, 4-amino-3-nitrophenol and (4-chloropyridin-2-yl)-N-methylcarboxamide were coupled using potassium bis(trimethylsilyl)amide

II

and K2CO3 in DMF to give 4-[(4-amino-3-nitrophenyl)oxy]-N-methylpyridine-2-carboxamide. Pd-catalyzed hydrogenation, followed by cyclization with 4-chloro-3-(trifluoromethyl)benzeneisothiocyanate in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide•HCl in THF provided the benzimidazole II. One thousand ninety-four compds. inhibited Raf kinase activity with IC50 < 5 µM in a Raf/Mek filtration assay or a biotinylated Raf screen. Thus, I and their pharmaceutical compns., which may comprise at least one addnl. agent, are useful for the treatment of Raf kinase mediated disorders, such as cancer (no data).

611220-90-7P 611221-14-8P 710353-65-4P,

N-Methyl-4-[[2-[[3-[2-(piperidin-1-yl)ethyl]phenyl]amino]-1H-benzimidazol5-yl]oxy]pyridine-2-carboxamide 710353-66-5P,

N-Methyl-4-[[1-methyl-2-[[3-[2-(piperidin-1-yl)ethyl]phenyl]amino]-1Hbenzimidazol-5-yl]oxy]pyridine-2-carboxamide 710353-67-6P,

4-[[6-Methoxy-1-methyl-2-[[3-[2-(piperidin-1-yl)ethyl]phenyl]amino]-1Hbenzimidazol-5-yl]oxy]-N-methylpyridine-2-carboxamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(Raf kinase inhibitor; preparation of substituted benzazoles as Raf kinase inhibitors for treatment of cancer)

RN 611220-90-7 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[[2-[[4-([1,4'-bipiperidin]-1' ylcarbonyl)phenyl]amino]-1-methyl-1H-benzimidazol-5-yl]oxy]-N-methyl (9CI) (CA INDEX NAME)

RN 611221-14-8 HCAPLUS
CN 2-Pyridinecarboxamide, N-methyl-4-[[1-methyl-2-[[4-[2-(1-piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]- (9CI) (CI INDEX NAME)

$$\begin{array}{c} N \\ N \\ N \\ N \\ N \\ N \\ Me \end{array}$$

RN 710353-65-4 HCAPLUS
CN 2-Pyridinecarboxamide, N-methyl-4-[[2-[[3-[2-(1-piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]- (9CI) (Ci INDEX NAME)

$$\begin{array}{c|c}
N & NH & NH & CH_2-CH_2-N \\
\hline
MeNH-C & NH & NH & CH_2-CH_2-N \\
\hline
0 & NH & NH & CH_2-CH_2-N \\
\hline
0 & NH & NH & CH_2-CH_2-N \\
\hline
0 & NH & NH & CH_2-CH_2-N \\
\hline
0 & NH & NH & CH_2-CH_2-N \\
\hline
0 & NH & NH & CH_2-CH_2-N \\
\hline
0 & NH & CH_2-CH_2-N \\$$

RN 710353-66-5 HCAPLUS
CN 2-Pyridinecarboxamide, N-methyl-4-[[1-methyl-2-[[3-[2-(1-piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]- (9CI) (CI INDEX NAME)

RN 710353-67-6 HCAPLUS

2-Pyridinecarboxamide, 4-[[6-methoxy-1-methyl-2-[[3-[2-(1-CN piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]-N-methyl- (9CI) (CA INDEX NAME)

ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN L14

2003:796477 HCAPLUS AN

DN 139:307759

Preparation of substituted benzazoles as Raf kinase inhibitors TI

Renhowe, Paul A.; Ramurthy, Savithri; Amiri, Payman; Levine, Barry IN Haskell; Poon, Daniel J.; Subramanian, Sharadha; Sung, Leonard; Fantl,

PA

Chiron Corporation, USA PCT Int. Appl., 259 pp. so

CODEN: PIXXD2

DΤ Patent

English LA

os GΙ

FAN.	CNT 2															
	PATENT :	KIND DATE				APPLICATION NO.							DATE			
PΙ				A1					2003	WO-U						
	W: .	AE, AG,														
		CO, CR,														
		GM, HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,
		LS, LT,	•									-				
		PH, PL,										ŢJ,	TM,	TN,	TR,	TT,
		TZ, UA,														
	RW:	GH, GM,	ΚE,	LS,	MW,	MZ,	SD,	SĻ,	SZ,	TZ,	ŪĠ,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG, KZ,	MD,	RU,	TJ,	TM,	ΑT,	ΒE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI, FR,														
		BF, BJ,														
								2003CA-2480638								
								2003AU-0226211								
	EP1499311							2003EP-0745683								
	R:	AT, BE,														PT,
		IE, SI,														
	BR20030											20030331				
					A 20050817 2003CN-0812193											
								2003JP-0579810								
	NZ5	35985			A 20070427 2003NZ-053598											
	IN2004K	N01433				2005										
	MX2004P	04PA09541 A				20050125 2004MX-PA09541										
	NO20040	04617		Α		2004										
	ZA-2004	,		Α		2006								20060308		
	JP20061	93533				2006			2006	JP-0	0961	43		2	0060	330
PRAI	2002US-			P			20020329									
		0579810		A3		2003										
	2003WO-			W		2003	0331									
os	MARPAT	139:3077	59													
C.T.																

$$A^{1} - N + X^{2} +$$

The title compds. [I; X1, X2 = N, NR4, O, S (with the provisos); Y = O, S; AB A1 = (un)substituted alkyl, cycloalkyl, aryl, etc.; A2 = (un)substituted heteroaryl; R1 = O, H, and R2 = NR5R6, OH; or CR1R2 = (un)substituted heterocycloalkyl, heteroaryl; R3 = H, halo, alkyl, alkoxy; R4 = H, OH, (di)alkylamino, alkyl; R5, R6 = H, (un)substituted alkyl, alkoxyalkyl, etc.; or R5 and R6 are taken together to form (un) substituted heterocyclyl or heteroaryl], useful for inhibition of Raf kinase activity in a human or animal subject, were prepared E.g., a 3-step synthesis of the benzimidazole II (starting from 4-amino-3-nitrophenol and (4-chloropyridin-2-yl)-Nmethylcarboxamide), was given. The compds. of examples 1-1094 showed a Raf kinase inhibitory activity at an IC50 of less than 5 μ M. A composition comprising the compound I is claimed. The new compds. compns. may be used either alone or in combination with at least one addnl. agent for the treatment of a Raf kinase mediated disorder, such as cancer. 611220-90-7P 611221-14-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of substituted benzazoles as Raf kinase inhibitors)

611220-90-7 HCAPLUS RN

2-Pyridinecarboxamide, 4-[[2-[[4-([1,4'-bipiperidin]-1'-ylcarbonyl)phenyl]amino]-1-methyl-1H-benzimidazol-5-yl]oxy]-N-methyl-CN(9CI) (CA INDEX NAME)

611221-14-8 HCAPLUS

2-Pyridinecarboxamide, N-methyl-4-[[1-methyl-2-[[4-[2-(1-CN piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]- (9CI) INDEX NAME)

```
MeNH-C N NH NH CH2-,CH2-N Me
```

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> => => b uspatall
FILE 'USPATFULL' ENTERED AT 18:03:53 ON 08 AUG 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'USPAT2' ENTERED AT 18:03:53 ON 08 AUG 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
=> d bib abs hitrn fhitstr 117
    ANSWER 1 OF 1 USPATFULL on STN
1.17
       2007:76306 USPATFULL
AN
ΤI
       Benzimidazolyl derivatives
       Stahle, Wolfgang, Ingelheim, GERMANY, FEDERAL REPUBLIC OF
IN
       Buchstaller, Hans-Peter, Griesheim, GERMANY, FEDERAL REPUBLIC OF
       Jonczyk, Alfred, Darmstadt, GERMANY, FEDERAL REPUBLIC OF
       Rautenberg, Wilfried, Reinheim, GERMANY, FEDERAL REPUBLIC OF
       Merck Patent GmbH, DARMSTADT, GERMANY, FEDERAL REPUBLIC OF, 64293
PA
       (non-U.S. corporation)
       US-20070066660
                               20070322
ΡI
                           A1
                               20041014 (10)
ΑI
       2004US-000577033
                           Α1
       2004WO-EP00011550
                               20041014
                               20060424 PCT 371 date
PRAI
       2003DE-0010349587
                           20031024
DT
       Utility
       APPLICATION
FS
LREP
       HELLER EHRMAN LLP, 1717 RHODE ISLAND AVE, NW, WASHINGTON, DC,
       20036-3001, US
       Number of Claims: 36
CLMN
       Exemplary Claim: 1
ECL
       No Drawings
DRWN
LN.CNT 2276
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention relates to the novel compounds of formula (I) wherein
       R.sup.1, R.sup.1, L, E, G, M, Q, U, R.sup.2, m, p and q are defined as
       in claim 1. The novel compounds are tyrosinkinase inhibitors, especially
       TIE-2 inhibitors, and Raf kinase inhibitors and can be used in the
       treatment of tumors.
                               ##STR1##
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     851677-12-8P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-
      (pyridin-4-yloxy)phenyl]amine 851677-13-9P,
      [4-(Pyridin-4-yloxy)phenyl](6-trifluoromethyl-1H-benzimidazol-2-yl)amine
      851677-14-0P, (6-Methyl-1H-benzimidazol-2-yl)[4-(pyridin-4-
      yloxy)phenyl]amine 851677-15-1P, (5-Chloro-4-methyl-1H-
      benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine 851677-16-2P
        (4-Bromo-6-trifluoromethyl-1H-benzimidazol-2-yl) [4-(pyridin-4-
      yloxy)phenyl]amine 851677-17-3P, (4-Bromo-6-trifluoromethyl-1H-
      benzimidazol-2-yl) [4-(pyridin-3-yloxy)phenyl]amine 851677-18-4P
        (5,6-Dimethyl-1H-benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine
      851677-19-5P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-
      (pyridin-3-yloxy)phenyl]amine 851677-20-8P,
      (5,6-Dichloro-1H-benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine
      851677-21-9P, (5,6-Dichloro-1H-benzimidazol-2-yl)[4-(pyridin-3-
      yloxy)phenyl]amine 851677-22-0P, (5-Chloro-1H-benzimidazol-2-
      yl) [4-(pyridin-4-yloxy)phenyl]amine 851677-23-1P,
      (5-Chloro-1H-benzimidazol-2-yl) [4-(pyridin-3-yloxy)phenyl]amine
```

851677-24-2P, (4-Methyl-1H-benzimidazol-2-yl)[4-(pyridin-3-yloxy)phenyl]amine 851677-25-3P, (4-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-(pyridin-4-yloxy)phenyl]amine 851677-26-4P

```
(4-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-(pyridin-3-
      yloxy)phenyl]amine 851677-27-5P, (4,5-Dimethyl-1H-benzimidazol-
      2-yl) [4-(pyridin-4-yloxy)phenyl]amine 851677-28-6P,
      (5-Chloro-6-methyl-1H-benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine
      851677-29-7P, (5-Chloro-6-methyl-1H-benzimidazol-2-yl)[4-(pyridin-
      3-yloxy)phenyl]amine 851677-30-0P, [4,6-Bis(trifluoromethyl)-1H-
      benzimidazol-2-yl] [4-(pyridin-4-yloxy)phenyl]amine 851677-31-1P
       [4,6-Bis(trifluoromethyl)-1H-benzimidazol-2-yl][4-(pyridin-3-
      yloxy)phenyl]amine 851677-32-2P, [4-(Pyridin-3-yloxy)phenyl](6-trifluoromethyl-1H-benzimidazol-2-yl)amine 851677-33-3P,
      (6-Methyl-1H-benzimidazol-2-yl) [4-(pyridin-3-yloxy)phenyl]amine
      851677-34-4P, (4,5-Dimethyl-1H-benzimidazol-2-yl)[4-(pyridin-3-
      yloxy)phenyl]amine 851677-35-5P, (5-Chloro-4-methyl-1H-
      benzimidazol-2-yl) [4-(pyridin-3-yloxy)phenyl]amine 851677-36-6P
        (4-Methyl-1H-benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl] amine
      851677-37-7P, (5,6-Dimethyl-1H-benzimidazol-2-yl)[4-(pyridin-3-
      yloxy)phenyl]amine 851677-39-9P 851677-40-2P
      851677-44-6P, (6-Nitro-1H-benzimidazol-2-yl)[4-(pyridin-4-
      yloxy)phenyl]amine 851677-45-7P, 2-[4-(Pyridin-4-
      yloxy)phenylamino]-3H-benzimidazole-5-carboxlic acid methyl ester
      851677-48-0P, (4-Fluoro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-
      (pyridin-4-yloxy)phenyl]amine 851677-51-5P 851677-52-6P
        (preparation of benzimidazolyls as TIE-2 tyrosine kinase inhibitors for the
        treatment of tumors)
IT 851677-12-8P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-
      (pyridin-4-yloxy)phenyl]amine
        (preparation of benzimidazolyls as TIE-2 tyrosine kinase inhibitors for the
        treatment of tumors)
RN
     851677-12-8 USPATFULL
     1H-Benzimidazol-2-amine, 5-chloro-N-[4-(4-pyridinyloxy)phenyl]-6-
CN
       (trifluoromethyl) - (9CI) (CA INDEX NAME)
```

=> d bib abs hitstr l18 tot

```
ANSWER 1 OF 5 USPATFULL on STN
1.18
AN
       2005:75878 USPATFULL
       Novel derivatives of benzimidazole and imidazo-pyridine and their use as
TI
       medicaments
TN
       Poitout, Lydie, Le Kremlin Bicetre, FRANCE
       Brault, Valerie, Saint-Arnoult-En-Yvelines, FRANCE
       Sackur, Carole, Paris, FRANCE
       Roubert, Pierre, Paris, FRANCE
       Plas, Pascale, Chatillon, FRANCE
                           A1 20050324
ΡI
       US-20050065179
       2004US-000915920
                               20040811 (10)
                           A1
AΙ
       Continuation-in-part of Ser. No. US 504033, PENDING A 371 of
RLI
       International Ser. No. 2004WO-FR00000418, filed on 25 Feb 2004, UNKNOWN
PRAI
                           20030226
       2003FR-0000002320
       Utility
DT
       APPLICATION
FS
       MUSERLIAN, LUCAS AND MERCANTI, LLP, 475 PARK AVENUE SOUTH, 15TH FLOOR,
LREP
       NEW YORK, NY, 10016
CLMN
       Number of Claims: 43
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 4046
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       A compound of the formula
                                  ##STR1##
```

wherein the substituents are as defined in the specification and pharmaceutical salts thereof having a good affinity for sub-types of melanocortin receptors making them useful for treating diseases in which

such receptors are included such as pain, inflammatory conditions, etc.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 848577-67-3P

(preparation of benzimidazoles and imidazopyridines having affinity for melanocortin (MC), in particular MC4, receptors)

RN 848577-67-3 USPATFULL

CN 1H-Benzimidazole-6-carboxamide, N,N-bis(3-methylbutyl)-1-[3-(1-piperidinyl)propyl]-2-[[4-(1-piperidinylsulfonyl)phenyl]amino]- (9CI) (CA INDEX NAME)

L18 ANSWER 2 OF 5 USPATFULL on STN

AN 2004:268349 USPATFULL

Heterocyclic compounds and methods of use

Di Pietro, Lucian V., Gloucester, MA, UNITED STATES
Harmange, Jean-Christophe, Andover, MA, UNITED STATES
Askew, Benny C., JR., Newbury Park, CA, UNITED STATES
Elbaum, Daniel, Newton, MA, UNITED STATES
Germain, Julie, Medford, MA, UNITED STATES
Habgood, Gregory J., Merrimac, MA, UNITED STATES
Kim, Joseph L., Wayland, MA, UNITED STATES
Patel, Vinod F., Acton, MA, UNITED STATES
Potachman, Michele, Cambridge, MA, UNITED STATES

Potashman, Michele, Cambridge, MA, UNITED STATES van der Plas, Simon, Medford, MA, UNITED STATES

PI US-20040209892 A1 20041021 AI 2004US-000804915 A1 20040319 (10)

PRAI 2003US-000456691P 20030321 (60)

DT Utility

TI

FS APPLICATION

LREP AMGEN INC., U.S. Patent Operations/JWB, Dept. 4300, M/S 27-4-A, One Amgen Center Drive, Thousand Oaks, CA, 91320-1799

CLMN Number of Claims: 60 ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 6639

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Selected compounds are effective for prophylaxis and treatment of diseases, such as angiogenesis mediated diseases. The invention encompasses novel compounds, analogs, prodrugs and pharmaceutically acceptable salts thereof, pharmaceutical compositions and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like. The subject invention also relates to processes for making such compounds as well as to intermediates useful in such processes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 769960-08-9P

(drug candidate; preparation of benzimidazole, benzoxazole and benzothiazole derivs. as kinase inhibitors)

RN 769960-08-9 USPATFULL

```
ANSWER 3 OF 5 USPATFULL on STN
2004:159433 USPATFULL
1.18
AN
       Substituted benzazoles and methods of their use as inhibitors of Raf
TI
       kinase
       Amiri, Payman, Walnut Creek, CA, UNITED STATES
IN
       Fantl, Wendy, San Francisco, CA, UNITED STATES
       Levine, Barry Haskell, Lafayette, CA, UNITED STATES
       Poon, Daniel J., Oakland, CA, UNITED STATES
       Ramurthy, Savithri, Walnut Creek, CA, UNITED STATES
       Renhowe, Paul A., Danville, CA, UNITED STATES
       Subramanian, Sharadha, San Ramon, CA, UNITED STATES
       Sung, Leonard, Irvine, CA, UNITED STATES
ΡI
       US-20040122237
                           A1 20040624
                           A1 20030929 (10)
ΑI
       2003US-000675927
RLI
       Continuation-in-part of Ser. No. 2003US-000405945, filed on 31 Mar 2003,
       PENDING
PRAI
       2002US-000369066P
                           20020329 (60)
       Utility
DT
       APPLICATION
FS
       Chiron Corporation, Intellectual Property - R440, P.O. Box 8097,
LREP
       Emeryville, CA, 94662-8097
       Number of Claims: 86
CT.MN
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 9816
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       New substituted benz-azole compounds, compositions and methods of
AB
       inhibition of Raf kinase activity in a human or animal subject are
       provided. The new compounds compositions may be used either alone or in
       combination with at least one additional agent for the treatment of a
       Raf kinase mediated disorder, such as cancer.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
   611220-90-7P 611221-14-8P 710353-65-4P,
      N-Methyl-4-[[2-[[3-[2-(piperidin-1-yl)ethyl]phenyl]amino]-1H-benzimidazol-
      5-yl]oxy]pyridine-2-carboxamide 710353-66-5P,
      N-Methyl-4-[[1-methyl-2-[[3-[2-(piperidin-1-yl)ethyl]phenyl]amino]-1H-
      benzimidazol-5-yl]oxy]pyridine-2-carboxamide 710353-67-6P,
      4-[[6-Methoxy-1-methyl-2-[[3-[2-(piperidin-1-yl)ethyl]phenyl]amino]-1H-
      benzimidazol-5-yl]oxy]-N-methylpyridine-2-carboxamide
        (Raf kinase inhibitor; preparation of substituted benzazoles as Raf kinase
        inhibitors for treatment of cancer)
     611220-90-7 USPATFULL
RN
     2-Pyridinecarboxamide, 4-[[2-[[4-([1,4'-bipiperidin]-1'-
CN
       ylcarbonyl)phenyl]amino]-1-methyl-1H-benzimidazol-5-yl]oxy]-N-methyl-
       (9CI)
             (CA INDEX NAME)
```

RN 611221-14-8 USPATFULL

CN 2-Pyridinecarboxamide, N-methyl-4-[[1-methyl-2-[[4-[2-(1piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]- (9CI) (CA INDEX NAME)

RN 710353-65-4 USPATFULL

RN 710353-66-5 USPATFULL

CN 2-Pyridinecarboxamide, N-methyl-4-[[1-methyl-2-[[3-[2-(1-piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]- (9CI) (CA INDEX NAME)

RN 710353-67-6 USPATFULL

L18 ANSWER 4 OF 5 USPATFULL on STN

AN 2004:114780 USPATFULL

TI Substituted benz-azoles and methods of their use as inhibitors of Raf kinase

IN Renhowe, Paul A., Danville, CA, UNITED STATES
Ramurthy, Savithri, Walnut Creek, CA, UNITED STATES
Amiri, Payman, Lafayette, CA, UNITED STATES
Levine, Barry Haskell, Lafayette, CA, UNITED STATES
Poon, Daniel J., Oakland, CA, UNITED STATES
Subramanian, Skaradha, San Ramon, CA, UNITED STATES
Sung, Leonard, Irvine, CA, UNITED STATES
Fantl, Wendy, San Francisco, CA, UNITED STATES

PI US-20040087626 US----7071216 A1 20040506

AI 2003US-000405945

B2 20060704 A1 20030331 (10) PRAI 2002US-000369066P 20020329 (60)

DT Utility

FS APPLICATION

LREP CHIRON CORPORATION, Intellectual Property-R440, P.O. Box 8097,

Emeryville, CA, 94662-8097

Number of Claims: 86 CLMN ECL Exemplary Claim: 1

No Drawings DRWN

LN.CNT 7855

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

New substituted benz-azole compounds, compositions and methods of AB inhibition of Raf kinase activity in a human or animal subject are provided. The new compounds compositions may be used either alone or in combination with at least one additional agent for the treatment of a Raf kinase mediated disorder, such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 611220-90-7P 611221-14-8P

(preparation of substituted benzazoles as Raf kinase inhibitors)

RN 611220-90-7 USPATFULL

2-Pyridinecarboxamide, 4-[[2-[[4-([1,4'-bipiperidin]-1'-CN ylcarbonyl)phenyl]amino]-1-methyl-1H-benzimidazol-5-yl]oxy]-N-methyl-(CA INDEX NAME)

RN 611221-14-8 USPATFULL

2-Pyridinecarboxamide, N-methyl-4-[[1-methyl-2-[[4-[2-(1-CN piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]- (9CI) (CA INDEX NAME)

ANSWER 5 OF 5 USPAT2 on STN 2004:114780 USPAT2 L18

AN

TI Substituted benz-azoles and methods of their use as inhibitors of Raf kinase

Renhowe, Paul A., Danville, CA, UNITED STATES TN Ramurthy, Savithri, Walnut Creek, CA, UNITED STATES Amiri, Payman, Walnut Creek, CA, UNITED STATES Levine, Barry Haskell, Lafayette, CA, UNITED STATES Poon, Daniel J., Oakland, CA, UNITED STATES Subramanian, Sharadha, San Ramon, CA, UNITED STATES Sung, Leonard, Irvine, CA, UNITED STATES

Fantl, Wendy, San Francisco, CA, UNITED STATES

Hansen, Teresa, Danville, CA, UNITED STATES

McBride, Christopher, Oakland, CA, UNITED STATES Shafer, Cynthia M., El Sobrante, CA, UNITED STATES

Chiron Corporation, Emeryville, CA, UNITED STATES (U.S. corporation) PA

US----7071216 20060704 B2 PΙ ΑI 2003US-000405945 20030331 (10)

PRAI 2002US-000369066P 20020329 (60)

Utility DT FS GRANTED EXNAM Primary Examiner: Stockton, Laura L.

Shelton, Dennis K., Suh, Young J., Harbin, Alisa A. LREP

Number of Claims: 66 CLMN ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 6608

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

New substituted benz-azole compounds, compositions and methods of inhibition of Raf kinase activity in a human or animal subject are provided. The new compounds compositions may be used either alone or in combination with at least one additional agent for the treatment of a Raf kinase mediated disorder, such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 611220-90-7P 611221-14-8P

(preparation of substituted benzazoles as Raf kinase inhibitors)

RN 611220-90-7 USPAT2

2-Pyridinecarboxamide, 4-[[2-[[4-([1,4'-bipiperidin]-1'-CN ylcarbonyl)phenyl]amino]-1-methyl-1H-benzimidazol-5-yl]oxy]-N-methyl-(9CI) (CA INDEX NAME)

RN 611221-14-8 USPAT2

2-Pyridinecarboxamide, N-methyl-4-[[1-methyl-2-[[4-[2-(1-CN piperidinyl)ethyl]phenyl]amino]-1H-benzimidazol-5-yl]oxy]- (9CI) (CA INDEX NAME)

=> d his

Ll

L4

(FILE 'HOME' ENTERED AT 17:40:43 ON 08 AUG 2007)

FILE 'HCAPLUS' ENTERED AT 17:41:17 ON 08 AUG 2007 1 US20070066660/PN OR (US2006-577033 OR WO2004-EP11550 OR DE2003-

FILE 'REGISTRY' ENTERED AT 17:44:11 ON 08 AUG 2007

FILE 'HCAPLUS' ENTERED AT 17:44:11 ON 08 AUG 2007

TRA L1 1- RN : 52 TERMS L2

FILE 'REGISTRY' ENTERED AT 17:44:11 ON 08 AUG 2007

L3 52 SEA L2

4 L3 AND C19H12CLF3N4O

6 NCNC2-C6/ES AND NC5/ES AND 46.150.18/RID AND C19H12CLF3N4O L5

2 L5 NOT L4 L6

SAV TEM L4 J033ES/A

FILE 'HCAPLUS' ENTERED AT 17:48:38 ON 08 AUG 2007 L7

FILE 'REGISTRY' ENTERED AT 17:49:31 ON 08 AUG 2007

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STR
L8
              1 L8
L9
             40 L8 FULL
L10
                SAV TEM L10 J033C1/A
L11
             33 L10 AND L3
     FILE 'HCAPLUS' ENTERED AT 17:57:50 ON 08 AUG 2007
L12
              5 L10
L13
              1 L12 AND L1
L14
              4 L12 NOT L13
     FILE 'HCAOLD' ENTERED AT 18:03:14 ON 08 AUG 2007
1.15
     FILE 'USPATFULL, USPAT2' ENTERED AT 18:03:23 ON 08 AUG 2007
L16
              1 L16 AND L1
L17
              5 L16 NOT L17
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=> d bib abs hitstr 17
     ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
     2005:409508 HCAPLUS
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     142:463726
     Preparation of benzimidazolyls as TIE-2 tyrosine kinase inhibitors for the
TI
     Staehle, Wolfgang; Buchstaller, Hans-Peter; Jonczyk, Alfred; Rautenberg,
IN
     Wilfried
     Merck Patent G.m.b.H., Germany
     PCT Int. Appl., 105 pp.
SO
     CODEN: PIXXD2
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     Patent
     German
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                                             APPLICATION NO.
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     PATENT NO.
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     WO2005042520
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             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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     EP---1675849
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     2004WO-EP11550
                                 20041014
     MARPAT 142:463726
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$$\begin{array}{c|c} R & & & \\ & & \\ & & \\ N & \\ N & \\ H & \\ & & \\ R1 & \\ & & \\ R2 & \\ \end{array}$$

Title compds. I [R = (R1)m; R1 = (R1')p; R2 = (R2')q; m, p, q = 0-4; R1, R1' = Halo, OH, CN, etc.; L = CH2, CH2CH2, O, etc.; R2' = halo, OH, CO2H, etc.; E, G, M, Q, U = C or N atom with provisos] and their pharmaceutically acceptable salts and formulations were prepared For example, condensation of 4-(4-isothiocyanatophenoxy)puridine and 4-nitro-1,2-phenylenediamine afforded claimed benzimidazol II. In TIE-2 tyrosine kinase inhibition assays, 3-examples of compds. I exhibited IC50 values ranging from 5-40 x 10-7 mol/L. Compds. I are claimed to be useful as tyrosine kinase inhibitors in the treatment of tumors.

IT 851677-12-8P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-(pyridin-4-yloxy)phenyl]amine 851677-19-5P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-(pyridin-3-yloxy)phenyl]amine

ΙI

trifluoromethyl-1H-benzimidazol-2-yl) [4-(pyridin-3-yloxy)phenyl]amine 851677-25-3P, (4-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine 851677-26-4P, (4-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl) [4-(pyridin-3-yloxy)phenyl]amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of benzimidazolyls as TIE-2 tyrosine kinase inhibitors for the treatment of tumors)

RN 851677-12-8 HCAPLUS CN 1H-Benzimidazol-2-am

1H-Benzimidazol-2-amine, 5-chloro-N-[4-(4-pyridinyloxy)phenyl]-6-(trifluoromethyl)- (9CI) (CA INDEX NAME)

RN 851677-19-5 HCAPLUS

CN 1H-Benzimidazol-2-amine, 5-chloro-N-[4-(3-pyridinyloxy)phenyl]-6-(trifluoromethyl)- (9CI) (CA INDEX NAME)

RN 851677-25-3 HCAPLUS

CN 1H-Benzimidazol-2-amine, 4-chloro-N-[4-(4-pyridinyloxy)phenyl]-6-(trifluoromethyl)- (9CI) (CA INDEX NAME)

RN 851677-26-4 HCAPLUS

CN 1H-Benzimidazol-2-amine, 4-chloro-N-[4-(3-pyridinyloxy)phenyl]-6-(trifluoromethyl)- (9CI) (CA INDEX NAME)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'USPAT2' ENTERED AT 18:12:45 ON 08 AUG 2007 CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr 120

ANSWER 1 OF 1 USPATFULL on STN 1.20 2007:76306 USPATFULL AN TI Benzimidazolyl derivatives Stahle, Wolfgang, Ingelheim, GERMANY, FEDERAL REPUBLIC OF IN Buchstaller, Hans-Peter, Griesheim, GERMANY, FEDERAL REPUBLIC OF Jonczyk, Alfred, Darmstadt, GERMANY, FEDERAL REPUBLIC OF Rautenberg, Wilfried, Reinheim, GERMANY, FEDERAL REPUBLIC OF Merck Patent GmbH, DARMSTADT, GERMANY, FEDERAL REPUBLIC OF, 64293 PA (non-U.S. corporation) 20070322 ΡI US-20070066660 2004US-000577033 20041014 (10) ΑI 2004WO-EP00011550 20041014 20060424 PCT 371 date PRAI 2003DE-0010349587 20031024 DT Utility FS APPLICATION HELLER EHRMAN LLP, 1717 RHODE ISLAND AVE, NW, WASHINGTON, DC, LREP 20036-3001, US Number of Claims: 36 CLMN Exemplary Claim: 1 ECL DRWN No Drawings LN.CNT 2276

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to the novel compounds of formula (I) wherein R.sup.1, R.sup.1, L, E, G, M, Q, U, R.sup.2, m, p and q are defined as in claim 1. The novel compounds are tyrosinkinase inhibitors, especially TIE-2 inhibitors, and Raf kinase inhibitors and can be used in the treatment of tumors. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 851677-12-8P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl)[4-(pyridin-4-yloxy) phenyl] amine 851677-19-5P, (5-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl) [4-(pyridin-3yloxy)phenyl]amine 851677-25-3P, (4-Chloro-6-trifluoromethyl-1Hbenzimidazol-2-yl) [4-(pyridin-4-yloxy)phenyl]amine 851677-26-4P (4-Chloro-6-trifluoromethyl-1H-benzimidazol-2-yl) [4-(pyridin-3yloxy)phenyl]amine (preparation of benzimidazolyls as TIE-2 tyrosine kinase inhibitors for the

treatment of tumors)

851677-12-8 USPATFULL RN

CN

1H-Benzimidazol-2-amine, 5-chloro-N-[4-(4-pyridinyloxy)phenyl]-6-(trifluoromethyl) - (9CI) (CA INDEX NAME)

RN 851677-19-5 USPATFULL

1H-Benzimidazol-2-amine, 5-chloro-N-[4-(3-pyridinyloxy)phenyl]-6-CN (trifluoromethyl) - (9CI) (CA INDEX NAME)

RN 851677-25-3 USPATFULL

1H-Benzimidazol-2-amine, 4-chloro-N-[4-(4-pyridinyloxy)phenyl]-6-(trifluoromethyl)- (9CI) (CA INDEX NAME) CN

851677-26-4 USPATFULL RN

1H-Benzimidazol-2-amine, 4-chloro-N-[4-(3-pyridinyloxy)phenyl]-6-CN (trifluoromethyl) - (9CI) (CA INDEX NAME)

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(FILE 'USPATFULL, USPAT2' ENTERED AT 18:03:53 ON 08 AUG 2007)

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FILE 'HCAPLUS' ENTERED AT 18:12:25 ON 08 AUG 2007

FILE 'USPATFULL, USPAT2' ENTERED AT 18:12:45 ON 08 AUG 2007

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